

### REMARKS

The specification has been amended to remove an internet website reference. Thus, no new matter has been added.

The specification has been objected to for a vague definition of percent identity of nucleic acid molecules as given on page 8, line 23 of the specification.

Applicants respectfully submit that the claimed percent identity has been limited to a particular algorithm, namely Clustal, and has recited the parameters used, namely the default parameters noted on page 3 of the Office Action. . LASERGENE, Megalign, or GCG, etc. are simply interface programs. They are not algorithms.

As is stated in the paragraph bridging pages 8 and 9 of the specification, the LASERGENE interface program, and Megalign in particular, use the recited Clustal alignment method or algorithm. Thus, one of ordinary skill in the art who aligns sequences using the Clustal method at its default parameters would obtain reproducible results. Therefore, it is respectfully submitted that the description given in the specification is not vague regarding the definition of percent identities as claimed in the present invention.

Formal drawings will be submitted upon allowance of the subject application.

Claims 1, 9-15, 21, and 24-26 were rejected under 35 USC §112, second paragraph, on the ground that they fail to point out and distinctly claim the subject matter essentially for the reasons pointed out in the objection above. It is respectfully submitted that, as was discussed above, LASERGENE is an interface program that uses the Clustal method of alignment in its Megalign interface program. Therefore, it is believed that the specification and the claims distinctly support the use of Clustal, with its default parameters, for sequence alignment. The Clustal algorithm is widely used in the field by those skilled in the art and yields reproducible results.

Claims 14, 15, and 26 have been cancelled.

Claims 1, 9-15, 21, and 24-26 were rejected under 35 USC §112, first paragraph, as failing to "provide structural characteristics" necessary for one skilled in the art to recognize that they are in possession of the claimed invention.

One skilled in the art would know from the disclosure of the specification that the activity of the claimed invention could be assayed as shown in Example 7, and references such as Baldet et al. (1993) *Eur J Biochem* 217:479-485.

Furthermore, Figure 1 depicts an alignment of the sequences disclosed in the present invention showing extensive regions of sequence identity among the plant biotin synthases (these regions were not known prior to this disclosure since only a single plant sequence, namely *Arabidopsis*, was known prior to the present invention). In addition, the conserved iron binding site of the enzyme is underlined and italicized in the figure. This sequence element, i.e., structural characteristic, is a

found in all biotin synthases from bacteria to plants (see Weaver et al. (1996) *Plant Physiol* 110:1021-1028). It is believed that one skilled in the art would appreciate whether a polypeptide sequence in their possession would qualify as a plant biotin synthase using the disclosure of the present invention.

It is stated on page 7 of the Office Action that the disclosure in the specification "does not reasonably provide enablement for any polynucleotide from any biologic and man made source, having biotin synthase activity and 85% identity to SEQ ID NO:22 or 24". It is alleged that undue experimentation would be required to obtain biotin synthase sequences within the scope of the claimed invention.

It is respectfully submitted that the disclosure in Figure 1 is sufficient, coupled with standard molecular biology tools, for one skilled in the art to isolate and determine that they have obtained a biotin synthase sequence from a plant.

Claims 1, 9-15, 21, and 24-26 were rejected under 35 USC §102 (b) as being anticipated by Weaver et al. This reference is the publication associated with the Arabidopsis biotin synthase sequence (gi 1705463 in the specification).

Attention is kindly invited to Table 5 of the specification which shows that SEQ ID NOs:22 and 24 have 79.8% and 79.6% identity to the Arabidopsis sequence when aligned using the Clustal method of alignment recited in Claim 1. This is well below the 85% sequence identity limit set forth in the claims. Therefore, it is believed that the claimed invention is not anticipated by the sequence disclosed in the reference. Clustal

In view of the above discussion, it is believed that one skilled in the art could reproducibly determine that this sequence is distinct from the claimed invention using the Clustal method of alignment. It appears that the results set forth on page 9 of the Office Action were not obtained using the Clustal method with default parameters, therefore, Weaver et al. does not anticipate the claimed invention because it does not disclose each and every element of the claimed invention.

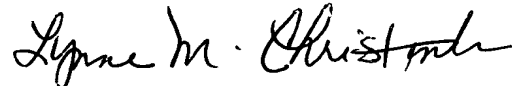
Applicants appreciate the indication in the Office Action that Claims 2-5 are allowed.

In view of the foregoing, it is respectfully submitted that the claims are now in form for allowance which allowance is respectfully solicited.

A petition for a three (3) month extension of time and a version with markings to show changes made accompany this response.

The Commissioner is authorized to charge Deposit Account 04-1928 (E. I. du Pont de Nemours and Company) for any requisite fees due or to credit any overpayment.

Respectfully submitted,



LYNNE M. CHRISTENBURY  
ATTORNEY FOR APPLICANTS  
REGISTRATION NO. 30,971  
TELEPHONE: 302-992-5481  
FACSIMILE: 302-892-1026

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**VERSION WITH MARKINGS TO SHOW CHANGES MADE**

In showing the changes, deleted material is shown surrounded by brackets and added material is shown by underlining.

**IN THE SPECIFICATION:**

Please replace paragraph on page 9, lines 6-28, with the following:

A "substantial portion" of an amino acid or nucleotide sequence comprises an amino acid or a nucleotide sequence that is sufficient to afford putative identification of the protein or gene that the amino acid or nucleotide sequence comprises. Amino acid and nucleotide sequences can be evaluated either manually by one skilled in the art, or by using computer-based sequence comparison and identification tools that employ algorithms such as BLAST (Basic Local Alignment Search Tool; Altschul et al. (1993) *J. Mol. Biol.* 215:403-410[; see also [www.ncbi.nlm.nih.gov/BLAST/](http://www.ncbi.nlm.nih.gov/BLAST/)]). In general, a sequence of ten or more contiguous amino acids or thirty or more contiguous nucleotides is necessary in order to putatively identify a polypeptide or nucleic acid sequence as homologous to a known protein or gene. Moreover, with respect to nucleotide sequences, gene-specific oligonucleotide probes comprising 30 or more contiguous nucleotides may be used in sequence-dependent methods of gene identification (e.g., Southern hybridization) and isolation (e.g., *in situ* hybridization of bacterial colonies or bacteriophage plaques). In addition, short oligonucleotides of 12 or more nucleotides may be used as amplification primers in PCR in order to obtain a particular nucleic acid fragment comprising the primers. Accordingly, a "substantial portion" of a nucleotide sequence comprises a nucleotide sequence that will afford specific identification and/or isolation of a nucleic acid fragment comprising the sequence. The instant specification teaches amino acid and nucleotide sequences encoding polypeptides that comprise one or more particular plant proteins. The skilled artisan, having the benefit of the sequences as reported herein, may now use all or a substantial portion of the disclosed sequences for purposes known to those skilled in this art. Accordingly, the instant invention comprises the complete sequences as reported in the accompanying Sequence Listing, as well as substantial portions of those sequences as defined above.

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